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Preliminary Amendment
Applicant(s): GANAPATHY et al.
Serial No. 10/718,359

Filed: November 20, 2003

For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-11. (Cancel)

12. (Currently amended) An isolated polypeptide, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the polynucleotide encodes a polypeptide demonstrating is capable of Na⁺-dependent transmembrane transport of citrate.

13. (Currently amended) The isolated polynucleotide polypeptide of claim 12, wherein the polynucleotide polypeptide comprises SEQ ID NO:6 [[5]].

14-19. (Cancel)

20. (Currently Amended) An isolated polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 75 [[35]]% sequence identity to SEQ ID NO:6, wherein the polynucleotide encodes a polypeptide demonstrating is capable of Na⁺-dependent transmembrane transport of citrate.

21. (Original) The isolated polynucleotide of claim 20, wherein the encoded Na⁺-dependent transmembrane transport of citrate is modulated by Li⁺.

22-26. (Cancel)

27. (Currently Amended) The isolated polynucleotide polypeptide of claim 20, wherein the encoded polypeptide demonstrating capable of Na⁺-dependent transmembrane transport of citrate demonstrates a requirement for requires multiple Na⁺ ions for transport coupling.

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28. (Currently Amended) The isolated polynucleotide polypeptide of claim 20, wherein the transmembrane transport of citrate is electrogenic.

29-35. (Cancel)

36. (Currently amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 80 [[35]]% identity with to SEQ ID NO:6 [[2]], wherein the polypeptide is a transmembrane transporter of citrate.

37-44. (Cancel)

45. (Currently amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least [[35%]] 85% sequence identity to SEQ ID NO:6, wherein the polypeptide demonstrates Na⁺-dependent transmembrane transport of citrate.

46. (Cancel)

47. (Currently Amendment) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 90 [[75]]% sequence identity to SEQ ID NO:6, wherein the polypeptide demonstrates Na⁺-dependent transmembrane transport of citrate.

48. (Cancel)

49. (Currently Amended) The [[An]] isolated polypeptide, of claim 20, the polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:1 under stringent hybridization conditions and wherein the polypeptide demonstrates transmembrane transport of citrate.

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50. (Currently Amended) The [[An]] isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 99 [[35]]% sequence identity to SEQ ID NO:6 [[8]], wherein the polypeptide demonstrates Na⁺-dependent transmembrane transport citrate.

51-56. (Cancel)

57. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% identity with SEQ ID NO:2 with an agent;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

58. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% sequence identity to SEQ ID NO:8, wherein the transmembrane citrate transporter polypeptide demonstrates Na⁺-dependent transmembrane transport of citrate with an agent;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

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wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

59. (Currently Amended) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 having at least 35% sequence identity to SEQ ID NO:6, wherein the transmembrane citrate transporter polypeptide demonstrates Na⁺-dependent transmembrane transport of citrate and with an agent wherein the encoded Na⁺-dependent transmembrane transport of citrate is stimulated by Li⁺;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

60-75. (Cancel)

76. (Currently Amended) A method of identifying an agent that modifies Na⁺-dependent transmembrane citrate transporter activity comprising:

contacting a host cell expressing a Na⁺-dependent transmembrane citrate transporter selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:12 of claim 12 with an agent;

measuring the citrate-induced inward electrical current into the host cell in the presence of agent; and

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comparing the citrate-induced inward electrical current into the host cell in the presence of the agent to the citrate-induced inward electrical current into the host cell in the absence of the agent;

wherein a decrease in the inward electrical current into the host cell in the presence of the agent indicates the agent is a blocker of Na^+ -dependent transmembrane citrate transporter activity;

wherein an increase in the inward electrical current into the host cell in the presence of the agent indicates the agent is a stimulator of Na^+ -dependent transmembrane citrate transporter activity.

77. (Currently Amended) A method of identifying an agent that serves as a substrate of a Na^+ -dependent transmembrane citrate transporter comprising:

contacting a host cell expressing a Na^+ -dependent transmembrane citrate transporter selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:12 of claim 12 with an agent; and

determining the entry of the agent into the cell via the Na^+ -dependent transmembrane citrate transporter in the presence of agent;

wherein entry of the agent via the Na^+ -dependent transmembrane citrate transporter indicates the agent is a substrate of a Na^+ -dependent transmembrane citrate transporter.

78. (New) A recombinant polypeptide, wherein the recombinant polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the recombinant polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

79. (New) The recombinant polypeptide of claim 78, wherein the recombinant polypeptide comprises SEQ ID NO:6.

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80. (New) A recombinant polypeptide comprising an amino acid sequence having at least 75% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na⁺-dependent transmembrane transport of citrate.

81. (New) The recombinant polypeptide of claim 80, wherein the encoded Na⁺-dependent transmembrane transport of citrate is modulated by Li⁺.

82. (New) A recombinant polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na⁺-dependent transmembrane transport of citrate.

83. (New) The recombinant polypeptide of claim 82, wherein the Na⁺-dependent transmembrane transport of citrate is modulated by Li⁺.